CASE REPORTS

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Tuberculous Mediastinal Lymphadenitis and Erythema Nodosum Simulating Polyarteritis Nodosa

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BIZARRE FORMS of tuberculosis, in particular extrapulmonary tuberculosis, are rarely seen nowadays in the United States, probably owing to the lower incidence of all types of tuberculosis, improved methods leading to early diagnosis, and possibly to more effective treatment. Erythema nodosum still occurs with relative frequency in the Scandinavian countries, although why this should be so is not apparent.

The following report of a case of tuberculous mediastinal lymphadenitis and erythema nodosum is presented because the clinical manifestations simulated those of polyarteritis nodosa and gave rise to speculation as to the pathogenesis.

REPORT OF A CASE

On Aug. 31, 1948, a 30-year-old Caucasian man was admitted to St. Vincent's Hospital, Los Angeles, with complaint of edema and aching of both ankles. While in England in 1945, the patient had had "primary atypical pneumonia" accompanied by pleural effusion of the right side. In 1942 an intracutaneous test with tuberculin had been carried out and there was positive reaction. The patient's mother had had excision of tuberculous cervical nodes in 1938. In the present illness, which had begun about a month before admittance to hospital, the patient had noted, in addition to the aching and edema of the ankles, an erythematous, nodular, and slightly tender eruption of the skin over the lower one-third of both legs, mild dyspnea upon exertion, intermittent respiratory wheezing, and a non-productive cough which had grown worse over a period of four months.

The patient was well developed and appeared to be well nourished. The temperature was 99° F., the pulse rate 76 per minute, respirations 20 per minute, and the blood pressure 150 mm. of mercury systolic and 102 mm. diastolic. Scattered high-pitched rhonchi on inspiration and expiration were noted throughout both lung fields. There was three-plus pitting edema of the ankles and feet and a faintly tender nodular eruption over the lower third of both legs. The nodules, a faint violaceous red, appeared to be in the dermis. Except for the elevation of blood pressure, no abnormalities were noted in the cardiovascular system.

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Reaction to a skin test with purified protein derivative No. 1 was faintly positive, to a coccidioidin skin test negative. Several specimens of the output of urine over 24-hour and 72-hour periods were examined. No acid-fast organisms were noted on smears, none grew on cultures, and results of guinea pig inoculation were negative. Complement fixation and precipitin reactions for Coccidioides immitis were likewise negative. In an anterior-posterior x-ray film of the chest both lung fields were observed to be clear, but there was some increase in bronchovascular markings. An electrocardiogram was normal except for sinus tachycardia. The hemoglobin content of the blood was 12 gm. per 100 cc. Erythrocytes numbered 6,200,000 per cu. mm., and leukocytes 11,600—23 per cent of them lymphocytes, 11 per cent monocytes, 2 per cent eosinophils, and 64 per cent neutrophils, of which 11 per cent were banded forms. The sedimentation rate (Westergren) was 63 mm. in one hour. The specific gravity of the urine was consistently 1.021 or more, and in an Addis test the urinary cell count was well within normal limits.

In the next two months the edema and skin eruption largely subsided, but when the patient was ambulatory or active the edema recurred and new crops of nodules appeared on the legs.

Two and a half months later, a report on biopsy specimens of skin and subcutaneous tissue taken from an involved area on the left leg was, "Non-specific arteritis resembling the involuting phase of polyarteritis nodosa." Several pathologists reviewed the specimens and all concurred in the diagnosis, except one who ventured an opinion of Boeck's sarcoidosis. The patient was advised to enter the hospital for investigation, but this he did not do until February, 1949.

On Feb. 13, 1949, the patient was readmitted with complaint of severe retrosternal and left shoulder-tip pain with paresthesia along the ulnar aspect of the left forearm and hand of five hours' duration. There had been similar bouts of less severe precordial pain lasting from two to three hours during the preceding two months. Edema and aching in the legs were still present. Nodules had reappeared on the anterior tibial surfaces of both legs. The clinical impression at this time was that the pain was caused by coronary arteritis with or without myocardial infarction as a result of polyarteritis nodosa. Serial electrocardiograms were made. One, taken six hours after admittance, was normal; in one taken on the fifth day of hospitalization there was evidence of posterior myocardial wall damage. In none of them, however, was there classical evidence of myocardial infarction. By the 22nd day the tracings were well within normal limits. During the first ten days, retrosternal pain recurred intermittently. In an x-ray film of the chest, definite widening of the upper mediastinum on both sides, greater on the right, was noted. In fluoroscopic examination, what appeared to

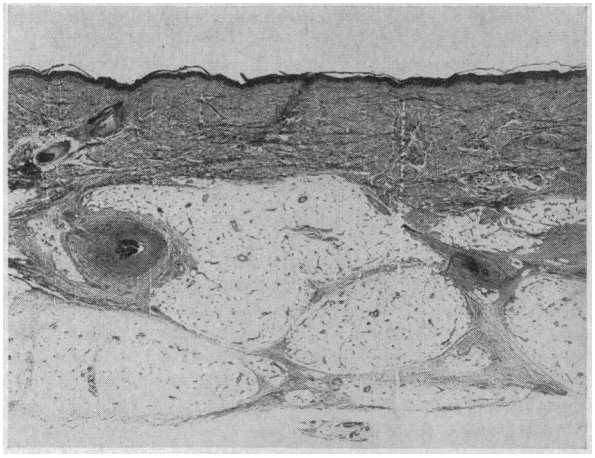

Figure 1.—Areas of involvement of epidermis and dermis (low power magnification).

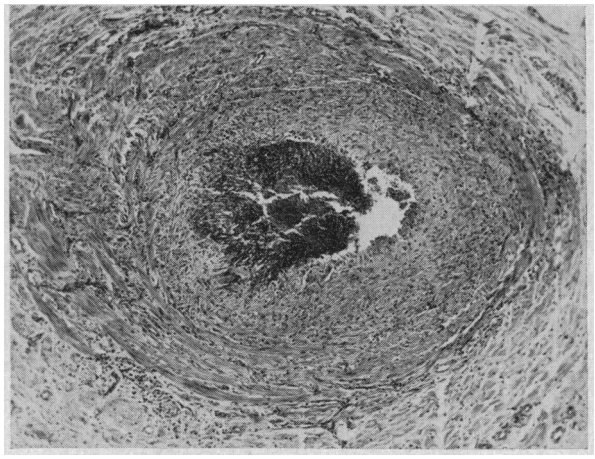

Figure 2.—The arteritis of the larger vessel seen in Figure 1 with a partially occluding thrombus.

be a tumor of the anterior mediastinum, lying to the right of the ascending aorta and not displacing the trachea, was observed. It was the opinion of a thoracic surgeon who was consulted that the mass was a large inflow tract (superior vena cava) consistent with the large build of the patient. Five weeks after admittance the patient was discharged, free of pain and with the dermal nodules on the legs almost cleared.

In the next nine months there was gradual clinical improvement, although the blood sedimentation rate remained between 28 mm. and 42 mm. in one hour. Pronounced fatigability also was noted and there were mild intermittent recurrences of ankle edema with a few scattered nodules on the legs. Specimens of skin, subcutaneous tissue and muscle were again examined and changes consistent with involuting polyarteritis nodosa were reported. The patient was given cortisone therapy from Jan. 25, 1950 to June 26, 1950. A total of 7.21 gm. of the hormone was given in that period. During this therapy the blood pressure rose from a pretreatment level of 135 mm. of mercury systolic and 98 mm. diastolic to as high as 178 mm. systolic and 120 mm. diastolic.

On April 24, 1950, the patient returned to the hospital with renal colic which was found to be caused by uric acid gravel secondary to hyperuricemia, probably as a result of cortisone. A second test with purified protein derivative No. 1 was carried out in May 1950, and the reaction was three plus, just short of necrosis. In an x-ray film taken at this time, slight change in the hilar outlines was observed. Soon afterward, a firm, discrete supraclavicular lymph node was noted for the first time and a specimen was removed for biopsy. Pathologic changes observed in it were reported typical of tuberculous lymphadenitis, including caseation. At autopsy of a guinea pig that was inoculated with material from the node, tuberculous lesions were noted.

The patient was then admitted to Barlow Sanatorium. During 90 days of modified bed rest and therapy with dihydrostreptomycin and paraminosalicylic acid the mediastinal shadow gradually diminished. No pathogenic organisms were observed in preliminary and follow-up examinations (including guinea pig inoculations) of specimens of sputum, gastric washings and urine. In repeated studies there was no evidence of activity to support the original diagnosis of polyarteritis nodosa. When last observed, the patient was well except for mild hypertension.

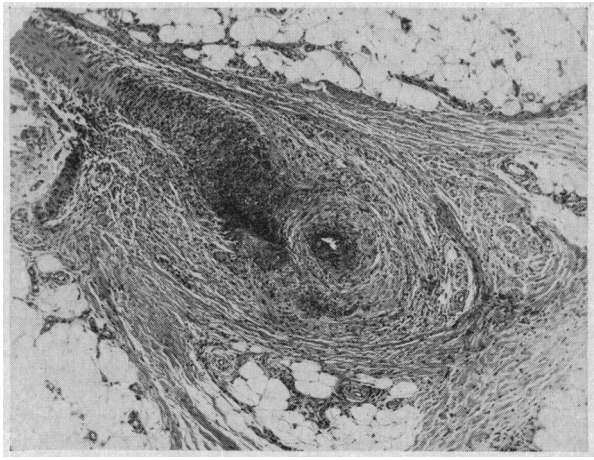

Figure 3.—The arteritis of the smaller vessel seen in Figure 1.

DISCUSSION

As time passes, the feeling is becoming more prevalent that polyarteritis nodosa is a generic entity with a variety of causes, all stemming primarily from hypersensitivity. Moreover the changes are at times pleomorphic. Arkin[1] in 1930 divided the lesions into four stages: the degenerative, acute inflammatory, granulation, and finally healed granulation tissue stage. The lesions in the various stages may vary broadly—from those resembling the lesions of the non-specific entity, nodular vasculitis on the one hand, to almost full-blown erythema induratum or other arterial lesions at the other extreme. Both polyarteritis nodosa and erythema nodosum, which is basically vasculitis, often have similar morphological criteria—lymphocytic, eosinophil, and neutrophil invasion of the vessel wall, occasional epithelioid and giant cells, thrombosis of the lumen, and, rarely, even minute foci of necrosis. The fact that polyarteritis nodosa often has many aspects in common with other kinds of vasculitis does not deny the existence of the clinical and pathological entity of polyarteritis nodosa. The point to be stressed is that the disease is not a rigidly circumscribed one, but rather a generic entity with many gradations varying from the mild to the fatal and classically described involvements, and at times easily confused with other forms of arteritis.

In the case herein reported, many of the clinical features of polyarteritis nodosa were present, and there was even biopsic evidence of the disease; yet some of the cardinal features were absent. At no time was renal, hepatic, splenic, or central and peripheral nervous system involvement observed. There is good reason to believe that the clinical episode of coronary arteritis with the associated peculiar, evanescent electrocardiographic changes was compatible with polyarteritis nodosa. Yet upon review of the electrocardiograms and considering the patient's clinical status at the corresponding times, it seems reasonable to believe that: (a) the cause was arteritis of a posteriorly located coronary branch, a counterpart of the arteritis observed in biopsy specimens; or, (b) that a tuberculous focus within the mediastinum adjacent to the pericardium and posterior wall of the heart could produce the same manifestations.

Wallgren[4] in Sweden observed that 70 per cent of cases of erythema nodosum in children were accompanied by evidence of active pulmonary disease, hilar changes as noted by x-ray, or other lesions, mainly of the lymphatic glands. In practically all the cases the disease was of the primary infection type. In the present case, the fact that the patient had a positive reaction to a tuberculin test in 1942 indicates that he must have had the primary infection years before the symptoms of the illness for which he was treated occurred. This is not at odds with the observation of the onset of erythema nodosum with recurrent exacerbations long after the time of initial infection, possibly as a result of secondary dissemination of the initial infection, or, conceivably, reinfection. Massini and Ramel[3] expressed the belief that recurrent erythema nodosum indicates a generalization of tuberculosis, tuberculous septicemia for example. Janussion,[3] on the other hand, felt that erythema nodosum is a sensitivity reaction—to primary tuberculosis in children, and to post-primary tuberculosis in adults. On the basis of Rich's[5] work it is known that resistance and sensitivity are two separate reactions on the part of the host to tubercle bacillus infection, and that the degrees of reaction do not necessarily correspond. The tuberculin skin test is based on hypersensitivity to the tubercle protein, and apparently in similar fashion erythema nodosum eruption arises as result of hematogenous spread of tubercle protein to hypergic skin. In the present case, of course, question arises as to why the reaction to the tuberculin skin test was but faintly positive during the acute phase of erythema nodosum eruption. The energy of overwhelming infection and minimal resistance is well known, but ordinarily a tuberculin skin test in the course of erythema nodosum due to tuberculosis causes exacerbation of the eruption. However, cases of erythema nodosum in which there were tuberculin-neutralizing properties in the serum have been reported.[2] Lofgren noted that the reaction to tuberculin was often stronger during the weeks following the acute eruption than while the lesions were present. Moreover he observed that in some cases there was no reaction or only faintly positive reaction to 0.0001 mg. of old tuberculin but pronounced positive reaction to 0.01 mg. of the substance. It does not seem too much to infer that perhaps the 0.00002 mg. of purified antigen contained in the purified protein derivative No. 1 used for skin testing in the present case was not a sufficient amount to evoke a highly positive reaction and exacerbation of the erythema nodosum eruption.

It is much easier to reconcile the biopsic observations with the outcome in the present case: Acid-fast organisms did not grow on cultures of material from the lesions and were not observed in stained specimens because the lesions were purely a hypersensitivity phenomenon secondary to tubercle protein and were not caused directly by viable organisms. Rich produced sterile hypersensitivity reactions in experimentally infected animals and also induced them by the injection of fractions of the tubercle bacillus. The presence of epithelioid and Langhans' giant cells, as well as the stromal involvement adjacent to the artery, in the case here reported might lead to suspicion that the condition was of granulomatous origin, but in the absence of bacilli and with the arteritic inflammatory changes more closely resembling those of involuting polyarteritis nodosa, the latter diagnosis was more credible.

SUMMARY

A case of tuberculous mediastinal lymphadenitis with erythema nodosum simulating polyarteritis nodosa is presented. An explanation is offered to reconcile the peculiar clinical manifestations on the basis of hypersensitivity, as well as to suggest that biopsy specimens of erythema nodosum may easily be confused with those of polyarteritis nodosa, a pleomorphic and generic entity.

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REFERENCES

1. Arkin, A.: A clinical and pathologic study of periarteritis nodosa, Am. J. Path., 6:401, 1930.

2. Kirby, P.: The etiology of erythema nodosum, British Journal of Radiology, 16:199, July 1943.

3. Lofgren, S.: Erythema Nodosum, P. A. Norstedt and Soner, Stockholm, 1946.

4. Miller, J. A., and Wallgren, A.: Pulmonary Tuberculosis in Adults and Children, Thos. Nelson & Sons, New York, 1939, pp. 126-130 and 153-154.

5. Rich, A. R.: The Pathogenesis of Tuberculosis, Chas. C. Thomas, Springfield, Ill., 1944. Chapters on hypersensitivity, the mechanism of hypersensitivity, application of the principles of pathogenesis.

Thrombocytopenic Purpura, Pregnancy and ACTH

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THROMBOCYTOPENIC PURPURA, although not common, has always caused great anxiety to obstetricians faced with the delivery of a patient with the disease and to surgeons contemplating splenectomy for such a patient.

In the past, massive blood transfusions and prayer have been the only answer to the problem. Recently, as the inherent dangers of transfusions have been better recognized, there has been a laudable search for techniques in which the use of blood and plasma is less important.

In this particular disease it seems that adrenocorticotropic hormone (ACTH) and cortisone will provide the answer. In the case of a woman with thrombocytopenic purpura who was at the full term of pregnancy, the drugs were used with dramatic effect before delivery and again before splenectomy.

REPORT OF A CASE

The patient, 36 years of age, gravida II, para I, was first observed July 11, 1951, with complaint of blood in the urine, first noted by her about one month previously in association with an attack of fever and aching diagnosed as "flu" by another physician. The hematuria had persisted and in addition the patient had noted rather severe bruising over her body, the presence of innumerable petechiae, especially below the waist, and excessive swelling of the legs. She stated, however, that in general she felt quite well.

The patient said that for years she had had eczema of the face and flexor surfaces of the arms and had used a coal tar preparation called "Zetar" for the past year. She had